AMENDMENTS TO THE CLAIMS

Listing of Claims:

NEW CLAIMS

1. (Original) Storage stable pharmaceutical formulation comprising at least two pharmaceutically active compounds in a diffusion matrix, characterized in that the matrix is determined with respect to its essential release characteristics by ethylcellulose or an ethylcellulose-based polymer and at least one fatty alcohol and that the active compounds are released from the substantially non-swellable diffusion matrix in a sustained, invariant and independent manner.

2. (Currently amended) Pharmaceutical formulation to claim 1, characterized in that the fatty alcohol comprises lauryl, myristyl, stearyl, cetylstearyl, ceryl and/or cetylalcohol[, preferably stearyl alcohol].

3. (Currently amended) Pharmaceutical formulation to claim [1 or] 2, characterized in that the formulation comprises ethylcellulose.

4. (Currently amended) Pharmaceutical formulation according to [one of the preceding claims] claim 3, characterized in that the formulation does not comprise relevant amounts of alkaline and/or water-swellable substances[, particularly derivatives of acrylic acid and/or hydroxyalkylcelluloses].

5. (Currently amended) Pharmaceutical formulation according to [one of the preceding claims] claim 4,
characterized in that the formulation comprises [common pharmaceutical excipients, particularly] fillers, lubricants, flowing agents and/or plasticizers.

6. (Currently amended) Pharmaceutical formulation according to claim 5, characterized in that the fillers are selected from the group comprising sugars, [preferably lactose, glucose and/or saccharose,] starches and hydrolysates thereof, [preferably micro-crystalline cellulose and/or cellactose,] sugar alcohols, [preferably sorbitol and/or mannitol,] poorly soluble calcium salts [, preferably calcium hydrogenphosphate, dicalciumphosphate or tricalciumphosphate] and/or povidone.

7. (Currently amended) Pharmaceutical formulation according to claim 5, characterized in that it comprises magnesium stearate, calcium stearate and/or calcium laureate and/or fatty acids[, preferably stearic acid as lubricant].

8. (Currently amended) Pharmaceutical formulation according to claim 5, characterized in that it comprises a flowing agent selected from the group consisting of highly dispersed silica, [preferably Aerosil®,] talcum, corn starch, magnesium oxide, magnesium and [/or] calciumstearate [as flowing agent].

9. (Currently amended) Pharmaceutical formulation according to claim 5, characterized in that it comprises dibutyl sebacate as a plasticizer.

10. (Currently amended) Pharmaceutical preparation according to [one of the preceding claims] claim 5, characterized in that the formulation can be stored over a period of at least two years under standard conditions (60% relative humidity, 25°C) in accordance with admission guidelines.

11. (Currently amended) Pharmaceutical preparation according to [one of the proceeding claims] claim 5, characterized in that it comprises as the pharmaceutically active compounds at least one opioid analgesic selected from the group comprising morphine, oxycodone, hydromorphone, propoxyphene, nicomorphine, dihydrocodeine, diamorphine, papaveretum, codeine, ethylmorphine, phenylpiperidine and derivatives thereof, methadone, dextropropoxyphene, buprenorphine, pentazocin, tilidine, tramadol and hydrocodone and at least one opioid antagonist, selected from the group comprising naltrexone, naloxone, nalmefene, nalorphine, nalbuphin, naloxonazinene, methylnaltrexone, ketylcyclazocine, norbinaltorphimine, naltrindol, 6-β-naloxol and 6-β-naltrexol.

12. (Currently amended) Pharmaceutical formulation according to claim 11, characterized in that the opioid analgesic and the antagonist are present in the form of their pharmaceutically acceptable and equally active derivatives, [such as the] free base, salts and the like[, preferably as the hydrochloride, sulfate, bisulfate, tatrate, nitrate, citrate, bitatrate, phosphate, malate, maleate, hydrobromide, hydroiodide, fumarate or succinate].

13. (Currently amended) Pharmaceutical formulation according to claim [11 or] 12, characterized in that the formulation comprises oxycodone and naloxone, and wherein oxycodone is present in an amount raging from about 10 mg to about 150 mg, [preferably from 10 to 80 mg] and naloxone is present in an amount ranging from about 1 mg to about 50 mg per unit dosage.

14. (Currently amended) Pharmaceutical formulation according to claim 13, characterized in that it comprises oxycodone and naloxone in a weight ratio ranging from about [maximal] 25:1, [preferably maximal 20:1, 15:1 and more preferably from 5:1, 4:1, 3:1, 2:1 and] to about 1:1.

15. (Currently amended) Pharmaceutical formulation according to claim [11 or] 12, characterized in that it contains oxycodone and naloxone with oxycodone being present in an amount ranging from about 10 mg to about 150 mg, [preferably from 10 to 80 mg] and naloxone is present in an amount ranging from about 1 mg to about 50 mg.

16. (Currently amended) Pharmaceutical formulation according to [one of the preceding claims] claim 13, characterized in that the formulation is in the form of a tablet, preferably a multi-layered tablet, a capsule, a dragée, a granulate and/or a powder.

17. (Currently amended) Pharmaceutical formulation according to claim 16, characterized in that the pharmaceutical preparation is suitable [or] for oral, nasal and/or rectal application.

18. (Currently amended) Pharmaceutical formulation according to [one of the preceding claims] claim 16, characterized in that the formulation is produced by build-up and/or break-down granulation[, preferably by spray granulation].

19. (Currently amended) Pharmaceutical formulation according to claim [1 or] 17, characterized in that the formulation is produced by extrusion.

20. (Original) Storage stable pharmaceutical formulation comprising at least two active compounds in a sustained release matrix, characterized in that the matrix is a substantially non-swellable diffusion matrix whose release characteristics are determined by amounts of ethylcellulose or an ethylcellulose-based polymer and at least one fatty alcohol as matrix components, and by extrusion or granulation of the matrix materials together with the amount of the active compounds for formulation of an active compound-containing matrix.

21. (Original) Storage stable pharmaceutical formulation according to claim 20, wherein the diffusion matrix is a substantially non-erosive matrix.

22. (Currently amended) Storage stable pharmaceutical formulation according to claim 20 [or 21], wherein the matrix material contains ethylcellulose.

23. (Currently amended) Storage stable pharmaceutical formulation according to claim 20 [to 22], wherein the matrix is formed by extrusion[, particularly by melt extrusion].

24. (Original) Storage stable pharmaceutical formulation having an effective amount of an opioid agonist and an opioid antagonist in a substantially non-swellable and non-erosive diffusion matrix, whose release characteristics are determined by amounts of ethylcellulose or an ethylcellulose-based polymer and at least one fatty alcohol.

25. (Currently amended) Storage stable pharmaceutical formulation according to claim 24 having an effective amount of oxycodone and naloxone, with oxycodone being present in an amount ranging from about 10 mg to about 150 mg, [preferably from 10 to 80 mg] and naloxone is present in an amount ranging from about 1 mg to about 50 mg per unit dosage.

26. (Currently amended) Storage stable pharmaceutical formulation according to claim 24 [or 25] having an effective amount of oxycodone and naloxone, wherein oxycodone and naloxone are present in a weight ratio ranging from about [maximal] 25:1, [preferably maximal 20:1, 15:1 and more preferably from 5:1, 4:1, 3:1, 2:1 and] to about 1:1.

27. (Currently amended) Method for producing a formulation according to [one of claims 1 to] claim 26,
characterized in that production is effected by granulation, preferably build-up and/or break-down granulation, [particularly preferably spray granulation is used].

28. (Currently amended) Method for producing a formulation according to [one of claims 1 to] claim 26,
being an extrusion method, wherein counter-rotating or co-rotating single or multiple screw extruders with/without kneading elements are used.

29. (Currently amended) Method according to claim 28, being an extrusion method wherein counter-rotating twin-screw extruders[, preferably without kneading elements,] are used.

30. (Currently amended) Method according to claim 28 [or 29], characterized in that the temperature of the heating zones of the extruders is [between] from about 20° [-] to about 120°C[, preferably between 50°-100°C, more preferably between 50°-90°C and even more preferably between 50°-70°C].

31. (Currently amended) Method according to claim 28 [to 30], characterized in that the diameter of the nozzle on the extruder is between about 1 mm to about 10 mm[, preferably between 2 to 8 mm and particularly preferably between 3 to 5 mm].

32. (Currently amended) Method according to claim 28 [to 31], characterized in that the resulting temperature in the extruder does not influence the stability of the active compounds.

33. (Currently amended) Method of producing a pharmaceutical dosage form for the treatment of opioid-induced side effects, characterized in that the pharmaceutical dosage form comprises a pharmaceutical formulation according to [one of the claims] claim 5 [1 to 10].

34. (Currently amended) Method according to claim 33, characterized in that the preparation is used for treatment of opioid-induced obstipation [and preferably for treatment of opioid-induced pruritus].

35. (Currently amended) Method of producing a pharmaceutical dosage form for the treatment of idiopathic syndromes, characterized in that the pharmaceutical dosage form comprises a pharmaceutical formulation according to [one of claims] claim 5 [1 to 10].

36. (Currently amended) Method according to claim 35, characterized in that the preparation is used for treatment of irritable bowel syndrome, [preferably for] treatment of idiopathic pruritus or pruritus due to cholestasia and/or renal dysfunction.

37. (Currently amended) Method according to [one of claims] claim 33 [to 36], characterized in that the matrix is a substantially non-swellable diffusion matrix whose release characteristics are determined by amounts of ethylcellulose or an ethylcellulose-based polymer and of at least one fatty alcohol.

38. (Currently amended) Method according to [one of claims 33 to] 37, characterized in that the preparation comprises [between approximately] from about 1 mg to about 50 mg naloxone, [preferably between approximately 5 to 30 mg naloxone and even more preferably between approximately 5 to 20 mg naloxone].

39. (Currently amended) Method according to [one of claims 33 to] claim 38, characterized in that naloxone is present in the form selected from the [of its] pharmaceutically acceptable and equally active derivatives[, such as] the free base, salts and the like[, preferably as the hydrochloride, sulfate, bisulfate, tatrate, nitrate, citrate, bitatrate, phosphate, malate, maleate, hydrobromide, hydroiodide, fumarate or succinate].

40. (Currently amended) Method according to [one of claims 33 to] claim 39, characterized in that the matrix is produced by extrusion.

41. (New) A pharmaceutical formulation according to claim 4, characterized in that the formulation does not comprise relevant amounts of derivatives of acrylic acid and/or hydroxyalkylcelluloses.

42. (New) A pharmaceutical formulation according to claim 6, characterized in that the fillers are selected from the group comprising lactose, glucose, saccharose, micro-crystalline cellulose, cellactose, sorbitol, mannitol, calcium hydrogenphosphate, dicalciumphosphate, tricalciumphosphate and povidone.

43. (New) A pharmaceutical formulation according to claim 7, characterized in that it comprises stearic acid.

44. (New) A pharmaceutical formulation according to claim 12, characterized in that the opioid analgesic and the antagonist are present in the form of the hydrochloride, sulfate, bisulfate, tartrate, nitrate, citrate, bitartrate, phosphate, malate, maleate, hydrobromide, hydroiodide, fumarate or succinate.

45. (New) A pharmaceutical formulation according to claim 13, characterized in that the formulation comprises oxycodone and naloxone, and wherein oxycodone is present in an amount raging from about 10 mg to about 80 mg and naloxone is present in an amount ranging from about 1 mg to about 50 mg per unit dosage.

46. (New) A pharmaceutical formulation according to claim 14, characterized in that it comprises oxycodone and naloxone in a weight ratio ranging from about 5:1 to about 1:1.

47. (New) A storage stable pharmaceutical formulation according to claim 23, wherein the matrix is formed by melt extrusion.

48. (New) A storage stable pharmaceutical formulation according to claim 25 having an effective amount of oxycodone and naloxone, with oxycodone being present in an amount ranging from about 10 mg to about 80 mg and naloxone being present in an amount ranging from about 1 mg to about 50 mg per unit dosage.

49. (New) A storage stable pharmaceutical formulation according to claim 26 having an effective amount of oxycodone and naloxone, wherein oxycodone and naloxone are present in a weight ratio ranging from about 5:1 to about 1:1.

50. (New) The method according to claim 30, characterized in that the temperature of the heating zones of the extruders is from about 50° to about 70°C.

51. (New) The method according to claim 31, characterized in that the diameter of the nozzle on the extruder is between about 3 mm to about 5 mm.

52. (New) The method according to claim 34, characterized in that the preparation is used for treatment of opioid-induced pruritus.

53. (New) The method according to 38, characterized in that the preparation comprises from about 5 mg to about 20 mg naloxone.

54. (New) The method according to claim 39, characterized in that naloxone is present in the form of the hydrochloride, sulfate, bisulfate, tartrate, nitrate, citrate, bitartrate, phosphate, malate, maleate, hydrobromide, hydroiodide, fumarate or succinate.